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Plasma-nor-adrenalin and adrenalin concentrations in feto-maternal blood: Their relations to feto-maternal endocrine levels, cardiotocographic and mechanocardiographic values, and umbilical arterial blood biochemical profilings

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Quantitative measurements of labor stress exerted on the fetus are thought to be difficult (SUREAU [14]). Although the fetal adrenal and sympathetic nervous systems are estimated to play a major role in regulating circulatory and metabolic functions under normal and abnormal circumstances during labor, previous studies have failed to document consistent changes in fetal adrenergic activities at the perinatal period. In pursuit of better indexes which might closely relate to the stress of labor, plasma concentrations of nor-adrenalin, adrenalin, cortisol, aldosterone, as well as, immunoreactive (I.R.) insulin were measured in both maternal and umbilical cord venous blood, and correlated with quantitative cardiotocographic and mechanocardiographic values, Apgar scores, and umbilical cord arterial blood biochemical profilings in high-risk pregnancies.

1 Materials and methods

During a year and a half period from September 1976, through February 1978, blood samples of 10 ml each were collected from maternal peripheral and umbilical cord veins immediately following deliveries in a total of 70 high-risk pregnancies at the Fukuoka University Hospital. The blood was collected in an iced centrifuge tube containing EDTA-2Na, and centrifuged at once for 20 minutes at 15,000 rpm at 4 °C. The plasma was removed, frozen and stored at 20 °C for further hormonal assays. Another 5 ml each of blood was withdrawn by a heparinized syringe from maternal peripheral vein, umbilical cord vein and artery. Determinations of blood Po_2, Pco_2, pH and base deficit were made by a Radiometer bloodgas analyzer. Enzymatic Analyses of glucose, lactate, pyruvate, glycerol, and so on were made by the methods described by BERGMEYER [1]. Finally, 3 ml of blood was collected in the iced centrifuge tube, and centrifuged at 4 °C. Plasma concentrations of free fatty acid (FFA) and inorganic phosphorous (P_i) were determined by WAKO-JUNYAKU Kit and FISKE-SUBBAROW method, respectively.

The method for measuring plasma nor-adrenalin and adrenalin concentrations was the trihydroxyindole method using $K_3Fe(CN)_6$ in the high-performance liquid chromatography, described by MATSUDA et al [9]. Catecholamine HPLC-Auto analyzer consisted of a piston-type pump (Kyowa-seimitsu KSU–P45H), a glass Zipax column (DuPont, 2 mm ± 70 cm), an auto-sample injector (HISSCO), an effluent exchanger, a proportioning pump (Technicon AIII), a fluorometer (Turner 111), and a process sequencer (Tokai B-90XA). A trace dose of epinine was added as an internal standard for correction of recovery rate. The sensitivity of measuring method for nor-adrenalin

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and adrenalin was 0.5 ng and 0.1 ng, respectively. The recovery rate of smaller Al_2O_3 was approximately 50%. Only 3 ml of plasma was necessary for these measurements in duplicate.

Another 1 ml of plasma was used for the measurements of maternal-fetal cortisol, aldosterone and I.R. insulin. Plasma cortisol was determined by a single antibody solid phase radioimmunoassay method using CEA-IRE-Sorin Cortisol · ^{125}I · RIA Kit. Plasma aldosterone was assayed by a radioimmunoassay without chromatography, using CEA-IRE-Sorin Aldosterone · ^{3}H Kit. I.R. insulin was measured by a dextran charcoal method using CEA-IRE-Sorin · ^{125} I Kit, as well. Cardiotocographic recordings were made by a Toitsu System Tocograph, PCS 260, on 55 pregnancies, and analyzed quantitatively by the dip area of SHELLEY and TIPTON [12], the bradycardie résiduelle of SUREAU [13], the bradycardia index of KOMAROMY [8], the prediction index of APGAR scores by SCHIFRIN and DAME [11], and the index of fetal welfare by TIPTON and SHELLEY [15]. Mechanocardiographic analyses were made from fetal ECG, PCG and ultrasonogram stored on a TEAC data recorder, R-70A, and visualized on San-ei Visigraph, 5L31. Statistical analysis was made using a computer, FACOM 230–25.

2 Results

2.1 Fetal and maternal hormonal levels

As shown on Tab. I, umbilical cord plasma concentrations of noradrenalin, adrenalin, cortisol, aldosterone and I.R. insulin were 78.3 ± 128.5 ng/dl, 8.2 ± 11.4 ng/dl, 33.8 ± 21.0 μg/dl, 50.8 ± 25.1 ng/dl and 1.46 ± 1.64 mU/dl, respectively, in average. Maternal plasma concentrations of those were 17.0 ± 12.7 ng/dl, 9.3 ± 10.3 ng/dl. 56.8 ± 22.1 μg/dl, 45.2 ± 20.7 ng/dl and 4.88 ± 6.62 mU/dl, respectively, indicating **a remarkably higher level in nor-adrenalin concentrations in fetal blood**. Those values in spontaneously delivered neonates whose APGAR scores were more than 8 are also shown on Tab. I. Tab. II demonstrates correlation coefficients between these hormonal concentrations. Fetal nor-adrenalin value was significantly ($p < 0.01$) correlated with fetal adrenalin and cortisol levels and maternal nor-adrenalin concentration. Fetal adrenal value was correlated with cortisol level ($p < 0.01$). Fetal cortisol concentration was also significantly ($p < 0.01$) correlated with fetal aldosterone and I.R. insulin, as well as, maternal cortisol value.

Tab. III indicates fetal and maternal hormonal levels at a different concentration of umbilical

Tab. I. Plasma concentrations of nor-adrenalin, adrenalin, cortisol, aldosterone and immunoreactive insulin in maternal peripheral and umbilical cord venous blood.

		Total	Spontaneously delivered neonates whose APGAR scores ⩾ 8
	Numbers	70	46
Parameters	(unit)	(Mean ± S.D.)	(Mean ± S.D.)
(Fetal Hormones)			
Nor-Adrenalin	(ng/dl)	78.3 ± 128.5	30.3 ± 49.8
Adrenalin	(ng/dl)	8.2 ± 11.4	4.7 ± 4.0
Cortisol	(μg/dl)	33.8 ± 21.0	30.6 ± 16.8
Aldosterone	(ng/dl)	50.8 ± 25.1	44.4 ± 22.6
I.R. Insulin	(mU/dl)	1.46 ± 1.64	1.50 ± 1.66
(Maternal Hormones)			
Nor-Adrenalin	(ng/dl)	17.0 ± 12.7	14.2 ± 9.4
Adrenalin	(ng/dl)	9.3 ± 10.3	9.2 ± 10.9
Cortisol	(μg/dl)	56.8 ± 22.1	57.0 ± 23.8
Aldosterone	(ng/dl)	45.2 ± 20.7	41.5 ± 20.4
I.R. Insulin	(mU/dl)	4.88 ± 6.62	4.33 ± 6.45

Tab. II. Correlation matrix between fetal and maternal hormone concentrations.

	Fetal Hormones				Maternal Hormones				
	Adr.	Corti.	Alds.	IRI	N.A.	Adr.	Corti.	Alds.	IRI
(Fetal Hormones)									
Nor-Adrenalin	*0.410*	*0.376*	*0.299*	–0.180	*0.427*	0.139	–0.038	0.200	0.051
Adrenalin		*0.371*	0.179	–0.181	0.228	0.118	0.116	*0.254*	–0.015
Cortisol			*0.562*	*–0.362*	0.146	–0.108	*0.355*	0.081	–0.166
Aldosterone				–0.131	*0.292*	–0.042	*0.379*	*0.767*	0.135
I.R. Insulin					0.050	–0.079	–0.174	–0.186	*0.496*
(Maternal Hormones)									
Nor-Adrenalin						*0.575*	0.210	*0.241*	0.177
Adrenalin							0.166	0.106	–0.117
Cortisol								*0.361*	0.059
Aldosterone									0.081

(n=70, d.f.=69, α=0.05 correlation limit: 0.234, α=0.01 correlation limit: 0.304)

Tab. III. Fetal and maternal hormonal concentrations at a different concentration of umbilical venous nor-adrenalin.

	Group	I	II	III	IV
	Nor-Adrenalin Concentrations	0–29 ng/dl	30–59 ng/dl	60–89 ng/dl	⩾ 90 ng/dl
	Numbers	32	19	5	14
Parameters	(unit)	(Mean ± S.D.)	(Mean ± S.D.)	(Mean ± S.D.)	(Mean ± S.D.)
(Fetal Hormones)					
Adrenalin	(ng/dl)	3.4 ± 2.7**	6.6 ± 4.3*	12.7 ± 3.1	19.9 ± 19.6
Cortisol	(μg/dl)	26.0 ± 13.9**	33.3 ± 15.8*	36.3 ± 18.6	51.0 ± 29.8
Aldosterone	(ng/dl)	39.4 ± 20.3**	52.6 ± 23.2	77.3 ± 30.4	67.2 ± 23.8
I.R. Insulin	(mU/dl)	1.61 ± 1.73	1.51 ± 1.62	3.30 ± 2.95**	0.66 ± 0.48
(Maternal Hormones)					
Nor-Adrenalin	(ng/dl)	12.5 ± 8.2**	15.2 ± 10.9*	28.0 ± 28.0	26.9 ± 13.7
Adrenalin	(ng/d)	8.5 ± 9.0	9.6 ± 13.2	6.7 ± 3.5	11.1 ± 9.8
Cortisol	(μg/dl)	55.2 ± 23.0	57.7 ± 21.1	75.0 ± 29.8	55.4 ± 20.6
Aldosterone	(ng/dl)	34.9 ± 17.0**	52.5 ± 20.0	63.0 ± 9.5	54.7 ± 20.9
I.R. Insulin	(mU/dl)	4.26 ± 6.12	5.49 ± 6.99	11.16 ± 16.37	4.18 ± 4.10

(*: $p < 0.05$ when compared with the group IV. **: $p < 0.01$ when compared with the group IV.)

blood nor-adrenalin. **With an elevation in fetal nor-adrenalin concentration, increased levels of fetal adrenalin, cortisol and aldosterone** as well as maternal nor-adrenalin and aldosterone, were observed. Suppression of I.R. insulin was also evident at nor-adrenalin concentrations more than 90 ng/dl.

2.2 Cardiotocographic and mechanocardiographic values

As shown on Tab. IV, fetal plasma concentration of nor-adrenalin was significantly ($p < 0.01$) correlated with dip area, bradycardie résiduelle, KOMAROMY index, and SCHIFRIN-DAMÉ index. Significant ($p < 0.01$) correlations were also observed between fetal catecholamine levels and mechanocardiographic values, such as pre-ejection period (PEP) and PEP/left ventricular ejection time (LVET) ratios at 40, 30 and 20 minutes prior to the deliveries of neonates, as partially demonstrated on Tab. IV. Tab. V demonstrates cardiotocographic and mechanocardiographic values at a different concentration of umbilical blood nor-adrenalin. **With an elevation in fetal nor-adrenalin levels, increased values were noted in dip area,**

Tab. IV. Correlation coefficients between maternal and fetal hormonal concentrations and cardiotocographic and mechanocardiographic values.

	Cardiotocographic Quantitative Values					Mechanocardiographic Values			
	Dip Area	Brady-cardie résiduelle	KOMA-ROMY Index	SCHIF-RIN-DAME Ind.	TIPTON-SHEL-LEY	PEP (-30 min)	PEP (-10 min)	PEP/ LVET (-30 min)	PEP/ LVET (-10 min)
(Fetal Hormones)									
Nor-Adrenalin	*0.856*	*0.607*	*0.496*	*0.667*	-0.247	*-0.578*	*-0.579*	*-0.435*	*-0.377*
Adrenalin	*0.277*	0.458	0.012	*-0.603*	-0.099	*-0.606*	*-0.564*	*-0.629*	-0.260
Cortisol	*0.318*	*0.287*	-0.033	-0.241	-0.268	*0.367*	-0.005	0.035	-0.142
Aldosterone	0.144	0.118	-0.110	*-0.525*	*-0.471*	0.093	0.147	0.148	-0.195
I.R. Insulin	-0.224	0.163	0.254	0.261	-0.119	0.247	-0.020	0.179	0.021
(Maternal Hormones)									
Nor-Adrenalin	0.064	0.231	0.038	-0.272	-0.241	0.091	-0.179	0.153	-0.065
Adrenalin	-0.157	-0.199	0.126	-0.075	*-0.289*	0.151	0.130	0.041	-0.063
Cortisol	-0.065	-0.019	-0.060	*-0.401*	-0.251	-0.223	-0.214	-0.283	-0.197
Aldosterone	0.046	0.035	-0.062	*-0.455*	-0.331	*0.306*	-0.026	0.031	-0.082
I.R. Insulin	-0.008	-0.107	*0.298*	-0.187	0.272	*0.384*	-0.143	*0.434*	*0.530*

(n=50, d.f. = 49, α=0.05 correlation limit: 0.276, α=0.01 correlation limit: 0.358)

Tab. V. Cardiotocographic quantitative values and mechanocardiographic parameters at a different concentration of umbilical venous nor-adrenalin.

	Group	I	II	III	IV
	Nor-Adrenalin Concentrations	0–29 ng/dl	30–59 ng/dl	60–89 ng/dl	⩾ 90 ng/dl
	Numbers	24	13	5	13
Parameters		(Mean ± S.D.)	(Mean ± S.D.)	(Mean ± S.D.)	(Mean ± S.D.)
(Cardiotocographic)					
Dip Area (SHELLEY-TIPTON)		72.8 ± 52.9	114.5 ± 67.8	100.5 ± 68.8	337.5 ± 310.5
Bradycardie résiduelle (SUREAU)		9.2 ± 10.3**	17.5 ± 15.5*	29.3 ± 28.0	66.5 ± 35.6
KOMAROMY Index (KRAUSE)		0.29 ± 0.24**	0.52 ± 0.28**	0.57 ± 0.48**	0.98 ± 0.70
SCHIFRIN-DAME Index		9.2 ± 0.7**	9.0 ± 0.9**	8.1 ± 1.7**	4.4 ± 3.3
TIPTON-SHELLEY Index		9.2 ± 0.9	8.5 ± 1.6	8.2 ± 3.0	7.6 ± 2.8
(Mechanocardiographic)					
PEP (Delivery – 30 Min.) (msec.)		65.9 ± 25.0**	71.0 ± 19.9**	54.4 ± 24.9	44.4 ± 18.6
PEP (Delivery – 20 Min.) (msec.)		65.4 ± 25.8**	74.3 ± 13.3**	50.7 ± 26.1	49.6 ± 17.5
PEP/LVET (Delivery – 30 Min.)		0.52 ± 0.17**	0.53 ± 0.16**	0.38 ± 0.22	0.39 ± 0.21
PEP/LVET(Delivery – 20 Min.)		0.52 ± 0.16**	0.50 ± 0.23**	0.35 ± 0.14	0.38 ± 0.21

(*: $p < 0.05$ when compared with the group IV. **: $p < 0.01$ when compared with the group IV.)

bradycardie résiduelle and Komáromy index, while SCHIFRIN-DAME index, TIPTON-SHELLEY index, PEP and PEP/LVET decreased. Average PEP at delivery minus 30 minutes was 66 msec at 0–29 ng/dl of nor-adrenalin concentrations, being 44 msec at the concentrations more than 90 ng/dl.

2.3 APGAR scores

APGAR scores were significantly ($p < 0.01$) correlated with fetal plasma concentrations of nor-adrenalin, cortisol and aldosterone (Tab. VI).

Tab. VI. Correlation coefficients with APGAR scores and mean APGAR scores at a different concentration of umbilical venous nor-adrenalin.

Parameters	Correlation Coefficients with APGAR Scores
(Fetal Hormones)	
Nor-Adrenalin	*-0.433*
Adrenalin	*-0.302*
Cortisol	*-0.467*
Aldosterone	*-0.366*
I.R. Insulin	0.101
(Maternal Hormones)	
Nor-Adrenalin	*-0.247*
Adrenalin	0.062
Cortisol	0.006
Aldosterone	*-0.235*
I.R. Insulin	0.060

(n= 70, d.f.= 69.
α= 0.05 correlation limit: 0.234,
α= 0.01 correlation limit: 0.304)

Nor-Adrenalin Concentrations	n	APGAR Scores (Mean + S.D.)
0–29 ng/dl	32	9.19 ± 0.54**
30–59 ng/dl	19	8.53 ± 1.38
60–89 ng/dl	5	8.33 ± 1.16
⩾ 90 ng/dl	14	7.21 ± 2.61

(**: $p < 0.01$ when compared with the group of ⩾ 90 ng/dl)

2.4 Umbilical arterial blood biochemical profilings

As demonstrated on Tab. VII, fetal plasma concentrations of nor-adrenalin, adrenalin, cortisol and aldosterone significantly ($p < 0.01$) correlated with several umbilical arterial blood biochemical parameters, such as $[H^+]$, [lactate] and [pyruvate]. Tab. VIII indicates umbilical arterial blood biochemical values at a different concentration of umbilical blood nor-adrenalin. **With an elevation of nor-adrenalin level, an increase in $[H^+]$, Pco_2, base deficit, [lactate] and [pyruvate] was observed.** When umbilical nor-adrenalin concentrations exceeded more than 90 ng/dl, $[H^+]$, Pco_2, base deficit, [lactate] and [pyruvate] increased to be 68 nM/L, 55 torr, 9.7 mEq/L, 3.9 mM/L and 146 μM/L, respectively, in average.

3 Comment

COMLINE and SILVER [5] reported that fetal chromaffin tissue in the adrenal medulla and sympathetic paraganglia produced a relatively larger proportion of total catecholamine content than in the adult. It has been suggested that nor-adrenalin concentration in the aortic paraganglia would be higher than in the adrenals. Noradrenalin contents in the heart, brain and other peripheral tissues were found to attain the adult level already at the second trimester (GREENBERG and LIND [6]). Placental passage of catecholamine would be minimal, and the disappearance of nor-adrenalin from fetal circulations was found to be slower than in the adult (SAARIKOSKI [10]). In response to asphyxia, nor-adrenalin would be mainly

Tab. VII. Correlation coefficients between maternal and fetal hormonal concentrations and umbilical arterial biochemical values.

	Umbilical Arterial Blood Biochemical Values								
	$[H^+]$	Pco_2	Po_2	Base Deficit	Lactate	Pyruvate	F.F.A.	Glycerol	P_i
(Fetal Hormones)									
Nor-Adrenalin	*0.631*	*0.444*	*-0.309*	*0.487*	*0.577*	*0.449*	0.068	*0.248*	0.161
Adrenalin	*0.506*	*0.440*	*-0.243*	*0.272*	*0.373*	*0.457*	0.091	-0.059	0.185
Cortisol	*0.486*	*0.329*	*-0.248*	*0.510*	*0.418*	*0.413*	0.230	0.188	0.162
Aldosterone	*0.423*	*0.293*	*-0.410*	*0.489*	*0.291*	*0.323*	0.097	-0.013	0.147
I.R. Insulin	-0.101	0.076	-0.018	-0.173	-0.129	0.056	-0.150	-0.161	-0.002
(Maternal Hormones)									
Nor-Adrenalin	*0.321*	0.136	-0.118	*0.378*	*0.341*	*0.280*	0.122	0.171	0.059
Adrenalin	0.063	-0.094	0.003	0.124	0.052	0.079	0.019	0.081	-0.016
Cortisol	-0.024	-0.001	*-0.280*	0.063	0.019	*0.281*	0.175	-0.149	-0.038
Aldosterone	*0.380*	*0.318*	*-0.480*	*0.416*	0.229	*0.300*	0.181	0.039	0.165
I.R. Insulin	0.051	0.076	-0.082	-0.049	-0.021	0.163	-0.150	-0.192	0.054

(n=70, d.f.=69, α=0.05 correlation limit: 0.234, α=0.01 correlation limit: 0.304)

Tab. VIII. Umbilical arterial blood biochemical values at a different concentration of umbilical venous nor-adrenalin.

	Group	I	II	III	IV
	Nor-Adrenalin Concentrations	0–29 ng/dl	30–59 ng/dl	60–89 ng/dl	⩾ 90 ng/dl
	Numbers	32	19	5	14
Parameters	(unit)	(Mean ± S.D.)	(Mean ± S.D.)	(Mean ± S.D.)	(Mean ± S.D.)
$[H^+]$	(nM/L)	48.4 ± 5.4**	53.9 ± 10.6**	58.0 ± 4.4	67.9 ± 13.1
Pco_2	(torr)	42.3 ± 7.0**	48.8 ± 11.6	54.3 ± 17.6	55.4 ± 17.6
Po_2	(torr)	22.6 ± 6.5*	17.7 ± 5.0	14.3 ± 7.5	17.5 ± 7.1
Base Deficit	(mEq/L)	4.4 ± 2.7**	5.2 ± 2.8**	8.7 ± 3.2	9.7 ± 5.4
Lactate	(mM/L)	1.83 ± 0.52**	1.95 ± 0.69**	2.40 ± 0.74	3.88 ± 2.16
Pyruvate	(μM/L)	100 ± 39**	104 ± 32**	145 ± 49	146 ± 43
Free Fatty Acid	(mEq/L)	124 ± 55*	310 ± 255	514 ± 487	426 ± 365
Glycerol	(μM/L)	201 ± 174	202 ± 51	235 ± 51	300 ± 261
Inorganic Phosph.	(mM/L)	1.28 ± 0.68	1.36 ± 0.32	1.45 ± 0.05	1.61 ± 0.47
Glucose	(mg/dl)	95.1 ± 34.8	101.1 ± 39.7	128.3 ± 51.7	88.3 ± 24.7

(*: $p < 0.05$ when compared with the group IV. **: $p < 0.01$ when compared with the group IV.

liberated from the chromaffin tissue under the influence of chemical and humoral stimulations (HERVONEN and KORKALA [7]). Severe asphyxia might result in a considerable depletion of catecholamine contents in the adrenal and extra-adrenal chromaffin tissues (CARMICHAEL [3], BRUNDIN [2]). The cardiovascular responses to hypoxia, such as an increase in heart rate, blood pressure and cardiac output as well as initial metabolic responses, such as shown in Fig. 1, are speculated to be associated with catecholamine releases.

Our results in this study clearly endorsed the above mentioned facts mainly evidenced by the animal experiments. In clinical situations, fetal adrenergic activities were assessed either by relatively insensitive urinary catecholamine excretion measurements or with estimation of circulating catecholamine levels by rather insensitive and non-specific methods. The development of sensitive high-performance liquid chromatography for the measurement of plasma catecholamine made these investigations possible with a relatively small

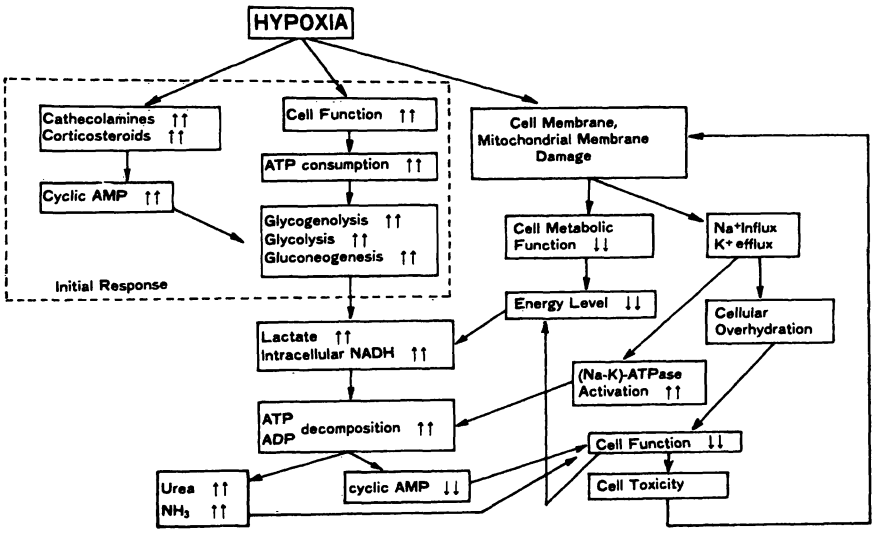

Fig. 1. Metabolic responses and adaptative mechanisms to hypoxia.

amount of blood samples. Possible harmful effects in both fetal circulatory and metabolic functions caused by an excessive liberation of nor-adrenalin from the chromaffin tissue was also evident in this study. **Nor-adrenalin concentrations more than 90 ng/dl in fetal circulation resulted in an increase in [H^+], base deficit, [lactate] and [pyruvate], indicating severe metabolic acidosis.** Plasma cortisol level was also described to be related with fetal distress as well as some roles in the initiation of parturition (CHALLIS and THORBURN [4]). However, it was found in this study that **the fetal catecholamine level was more correlated with cardiotocographic and mechanocardiographic parameters, Apgar scores, and umbilical cord blood biochemical profilings.**

Summary

The purpose of this study was to investigate the plasma concentrations of nor-adrenalin and adrenalin in umbilical cord blood and their relations with other feto-maternal hormonal levels, fetal cardiotocographic and mechanocardiographic values, and umbilical arterial blood biochemical profilings in pursuit of a better index which might closely relate to the stress of labor. A total of 70 high-risk pregnancies were studied. Plasma noradrenalin and adrenalin were measured by the THI method using a high-performance liquid chromatography. Radioimmunoassay of plasma cortisol, aldosterone and immunoreactive insulin were made. Cardiotocographic recordings were analyzed quantitatively by the dip area, bradycardie résiduelle, KOMAROMY index, SCHIFRIN-DAME index and TIPTON-SHELLEY index. Mechanocardiogram was obtained from fetal ECG, PCG and ultrasonogram. Determinations of bloodgas and biochemical values were done using a bloodgas analyzer and enzymatic analysis. The following data were obtained.

(1) Fetal plasma concentrations of nor-adrenalin, adrenalin, cortisol, aldosterone and insulin were 78.3 ng/dl, 8.2 ng/dl, 33.8 μg/dl, 50.8 ng/dl and 1.46 mU/dl, respectively in average. Maternal concentrations of these hormones were 17.0, 9.3, 56.8, 45.2 and 4.88, respectively, indicating **a remarkably higher level in nor-adrenalin in the fetal blood** (Tab. I). Although fairly poor correlation was found between fetal and maternal hormonal levels, fetal nor-adrenalin levels were significantly correlated with fetal adrenalin and cortisol, as well as, maternal nor-adrenalin values (Tab. II). With an increase in fetal nor-adrenalin level more than 90 ng/dl, an increase in fetal adrenalin, cortisol and aldosterone as well as suppression of insulin were found (Tab. III). (2) **Fetal plasma nor-adrenalin concentration was significantly correlated with the dip area,** bradycardie résiduelle, KOMAROMY index, SCHIFRIN-DAME index, PEP and PEP/LVET ratio (Tab. IV). With an increase in fetal nor-adrenalin level, an increase in dip area, bradycardie résiduelle and KOMAROMY index, as well as a decrease in cardiotocographic APGAR-predicting indexes, PEP and PEP/LVET ratio were noted (Tab. V).

(3) Fetal plasma concentrations of nor-adrenalin, adrenalin, cortisol and aldosterone were correlated with neonatal APGAR scores (Tab. VI) as well as umbilical arterial [H^+], Pco_2, Po_2, base deficit, [lactate] and [pyruvate] (Tab. VII). When umbilical cord nor-adrenalin value exceeded more than 90 ng/dl, [H^+], Pco_2, base deficit and [lactate] increased to be 68 nM/L, 55 torr, 9.7 mEq/L and 3.9 mM/L, respectively in average (Tab. VIII). **In response to the stress of labor, nor-adrenalin would be liberated from the chromaffin tissue in fetal adrenal medulla and sympathetic paraganglia.** As a result, initial fetal response in both cardiovascular and metabolic functions would be observed. However, **when fetal plasma concentration of nor-adrenalin exceeded more than 90 ng/dl, possible harmful effects might be followed.** Plasma concentration of nor-adrenalin in fetal circulation would be a better index of the intrapartum stress exerted on the fetus.

Keywords: Adrenalin, aldosterone, anoxia, bloodgas, cardiotocography, cortisol, fetus, mechanocardiography, nor-adrenalin, stress.

Zusammenfassung

Noradrenalin- und Adrenalinspiegel im feto-maternalen Blut in Relation zum übrigen Hormonhaushalt sowie zu Informationen aus dem Cardiotokogramm bzw. Mechanocardiogramm und zu biochemischen Blutprofilen aus der Nabelschnurarterie

Ziel dieser Untersuchung war die Bestimmung der Plasmakonzentrationen von Noradrenalin und Adrenalin im Nabelschnurarterienblut sowie deren Zusammenhang mit der Konzentration weiterer Hormone, dem Cardiotokogramm, dem Mechanocardiogramm und den Ergebnissen biochemischer Analysen des Nabelschnurblutes. Unsere Absicht war dabei, die Abhängigkeit der Hormonkonzentrationen vom Geburtsstress herauszustellen.

Wir untersuchten insgesamt 70 Risikoschwangerschaften. Die Noradrenalin- und Adrenalinkonzentrationen im Plasma wurden über die Flüssigkeitschromatographie unter Benutzung der THI-(=Trihydroxyindol)Methode bestimmt. Die werte für Cortisol, Aldosteron und immunreaktives Insulin haben wir über den Radioimmunassay gewonnen.

Die quantitative Analyse der Cardiotokogramm erfolgte über die Bestimmung der Dezelerationsflächen, der Bradycardie résiduelle, des KOMAROMY-Index, des SCHIFRIN-DAME-Index und des TIPTON-SHELLEY-Index. Das Mechanogramm erhielten wir üüber Informationen aus dem ECG, PCG und dem Ultraschallverfahren. Blutgaswerte und biochemische Analysen wurden unter Benutzung eines Blutgasanalysators erstellt. Darüberhinaus wurden die Proben enzymatisch analysiert. Wir erhielten folgende Ergebnisse:

1. Die fetale Plasmakonzentration betrug von Noradrenalin 78.3 ng/dl, von Adrenalin 8.2 ng/dl, von Cortisol 33.8 µg/dl, von Aldosteron 50.8 ng/dl und von Insulin 1.46 mU/dl; es handelt sich jeweils um Durchschnittswerte. Die Konzentration der genannten Hormone im mütterlichen Blut lag bei 17,0 ng/dl, 9.3 ng/dl, 56.8 µg/dl, 45.2 ng/dl und 4.88 mU/dl; d.h., **der Noradrenalinspiegel liegt im fetalen Blut wesentlich höher** (Tab. I).
   Während insgesamt gesehen mütterlicher und fetaler Hormonspiegel nur geringfügig korrelierten, fand sich ein signifikanter Zusammenhang zwischen fetaler Noradrenalinkonzentration und fetalem Adrenalin- bzw. Cortisolgehalt, der sich auch in Bezug auf den mütterlichen Noradrenalinspiegel korrelativ verhielt (Tab. II). Stieg der fetale Noradrenalinspiegel über 90 ng/dl, so konnte eine Zunahme von Adrenalin, Cortisol und Aldosteron sowie ein herabgesetzter Insulinspiegel im fetalen Blut gefunden werden (Tab. III).
2. **Wir fanden einen signifikanten Zusammenhang zwischen fetaler Plasma-Noradrenalinkonzentration und der Dezelerationsfläche**, der Bradycardie résiduelle, dem KOMAROMY-Index, dem SCHIFRIN-DAME-Index sowie der Dauer der Anspannungs- bzw. Austreibungsphase des linken Ventrikels. (Tab. IV). Mit Anstieg des fetalen Noradrenalinspiegels nahmen die Dezelerationsfläche, die Bradycardie résiduelle und der KOMAROMY-Index zu. Auf der anderen Seite wurden eine kürzere Anspannungsphase sowie ein herabgesetztes Verhältnis von Anspannungs- zu Austreibungszeit beobachtet. Auch die anderen aus dem Cardiotokogramm abgeleiteten Indices zeigten kleinere Werte (Tab. V).
3. Wir korrelierten die fetalen Plasmakonzentrationen von Noradrenalin, Adrenalin, Cortisol und Aldosteron mit den APGAR-Werten (Tab. VI) sowie mit der H^+-Konzentration, dem pCO_2 und pO_2, dem Basenmangel und der Lactat- bzw. Pyruvatkonzentration (Tab. VII. Wenn der Noradreanlinspiegel im Nabelschnurarterienblut über 90 ng/dl lag, stiegen die Werte für $[H^+]$, pCO_2, Basenmangel und Lactatkonzentration durchschnittlich auf 68 nM/dl, 55 Torr, 9.7 mÄq/l und 3.9 mM/l (Tab. VIII).

Als Antwort auf den geburtsbedingten Stress könnte Noradrenalin aus dem chromaffinen Gewebe des fetalen Nebennierenmarks und den Paraganglien freigesetzt werden. Im Ergebnis bedeutet das eine Erhöhung der cardiovaskulären und metabolischen Leistungen. **Wenn jedoch die Noradrenalinkonzentration 90 ng/dl übersteigt, treten,** wie man gesehen hat, **ungünstige Effekte in den Vordergrund.** Über die Noradrenalinkonzentrationen im fetalen Kreislauf sind gute Hinweise auf geburtsbedingte Stresszustände zu erhalten.

Schlüsselwörter: Adrenalin, Aldosteron, Anoxie, Blutgaswerte, Cardiotokographie, Cortisol, Fet, Mechanocardiographie, Noradrenalin, Stress.

Résumé

La nor-adrénaline du plasma et les concentrations d'adrénaline dans le sang foeto-maternel: Leurs relations avec les niveaux endocriniers foeto-maternels, les valeurs cordiotocographieues et mécanocardiographiques, et les profils biochimiques du sang artériel ombilical

La présente recherche a en pour objet d'étudier les concentrations de la nor-adrénaline et de l'adrénaline du sang du cordon ombilical et leurs relations avec d'autres niveaux hormonaux materno-foetaux, les valeurs cardiotocographiques et mécanocardiographiques foetales et les profils biochimiques du sang artériel ombilical en vue d'obtenir un meilleur index pour le stress de la délivrance. Un total de 70 délivrances à haut risque ont été étudiées. De la nor-adrénaline et de l'adrénaline dans le plasma ont été mesurées par la méthode THI en employant une chromatographie liquide moderne. On a procédé à des radioimmunoessais du cortisol, de l'aldostérone et de l'insuline immunoréactive dans le plasma. Les enregistrements cardiotocographiques ont été analysés quantitativement à l'aide de l'aire d'inclinaison, de la bradycardie résiduelle, de l'index de KOMAROMY, de l'index de SCHIFRIN-DAME et de l'index de TIPTON-SHELLEY. Le mécanocardiogramme a été obtenu a partir de l'ecg., du pcg. et de l'ultrasonogramme foetaux. Les déterminations des valeurs du gaz sanguin et biochimiques ont été faites en employant un analyserer du gaz sanguin et l'analyse enzymatique. Les résultas obtenus sont les suivants:

(1) Les concentrations dans le plasma foetal de la nor-adrénaline, de l'adrénaline, du cortisol, de l'aldostérone, et de l'insuline ont été respectivement et en moyenne de 78.3 ng/dl, 8'2 ng/dl, 33.8 µg/dl, 50'8 ng/dl et 1'46 mU/dl. Les concentrations dans le plasma maternal de ces hormones ont été respectivement de 17.0, 9.3, 56.8, 45.2 et 4.88, ce qui indique un niveau remarquablement plus élevé de la nor-adrénaline dans le sang foetal (Tab. I). Bien que la corrélation ait été assez faible entre les niveaux hormonaux du foetus et de la mère, les niveaux de la nor-adrénaline du foetus ont été en correlation significative avec les concentrations de l'adrénaline foetale, du cortisol foetal et de la nor-adrénaline maternelle (Tab. II). Avec une augumentation de plus de 90 ng/dl du niveau de la nor-adrénaline foetale, on a observé un accroissement d'adrénaline, du cortisol et d'aldostérone foetale ainsi qu'une suppression de l'insuline (Tab. III).

(2) **La concentration de la nor-adrénaline dans le plasma foetal a été en correlation significative avec l'aire d'inclinaison,** la bradycardie résiduelle, l'index de

KOMAROMY, l'index de SCHIFRIN-DAME, le PEP et la rapport PEP/LVET (Tab. IV). Avec une augmentation du niveau de la nor-adrénaline foetale, on a relevé un accroissement d'aire d'inclinaison, de bradycardie résiduelle et d'index de KOMAROMY ainsi qu'une décroissance des index de CTG-APGAR-prédiction, du PEP et du rapport PEP/LVET (Tab. V).

(3) Les concentrations de la nor-adrénaline, de l'adrénaline, du cortisol et de l'aldostérone dans le plasma foetal ont été en correlation significative avec les scores d'APGAR (Tab. VI) et aussi avec l'$[H^+]$, le Pco_2, le Po_2, le déficit basique, le [lactate] et le [pyruvate] arteriels ombilicaux (Tab. VII). Quand la valeur de la nor-adrénaline du cordon ombilical a dépassé 90 ng/dl, l'$[H^+]$, le Pco_2, le déficit basique et le [lactate] ont augmenté [pour atteindre respectivement et en moyenne] 68 nM/L, 55 torr, 9.7 mEq/L et 3'9 mM/L (Tab. VIII).

Eu réaction au stresse de la délivrance, [il semble donc que] la nor-adrénaline soit libérée du tissu chromaffin dans la médulle adrénale et le paraganglion sympathétique foetals.

A la suite de cela on a observé une réaction foetale initiale dans les deux fonctions cardiovascularie et métabolique. Toutefois, **des effets nocifs pourraient se produire quand la concentration de la nor-adrénaline dans le plasma foetal dépasse 90 ng/dl'** La concentration de la nor-adrénaline dans le plasma du sang foetal pourrait être un meilleur index du stress intrapartum exercé sur le foetus.

Mots-clés: Adrénaline, aldostérone, anoxie, cardiotocographie, cortisol, foetus, gaz sanguin, mécanocardiographie, nor-adrénaline, stress.

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